UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,208	07/20/2001	Jiro Hitomi	MM4454	4894

1109 7590 03/17/2005

ANDERSON, KILL & OLICK, P.C.
1251 AVENUE OF THE AMERICAS
NEW YORK,, NY 10020-1182

EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/910,208	HITOMI ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2004 and 20 July 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-24* is/are pending in the application.

4a) Of the above claim(s) *24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/568,310.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 18-24 are pending.

2. It is noted that the transmittal paper submitted on 07/20/01 has canceled claims 1-17. Therefore, the restriction requirements mailed on 10/05/04 would have only two Groups, Group IV and V, remain.

3. Applicant's election with traverse of Group IV, claims 18-23, drawn to an antibody with binding affinity to a protein encoded by SEQ ID NO: 1 or 12 and a method for producing and the protein encoded by SEQ ID NO: 12 as the species filed on 12/22/04, is acknowledged.

Applicant's traversal is on the grounds that the restriction did not include claim 24 with claims 18-23. Further, Applicant traverse the restriction as it applies to Groups IV and V on the basis that there is no undue burden on the Examiner. This is not found persuasive because the Groups IV/V are related as product and process of using. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody of Group III can be used for affinity purification, in addition to the assay recited. Therefore the antibody and the assay method using the antibody are distinct and independent, and searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group. Further, a prior art search also requires a literature search. It is an undue burden for the examiner to search more than one invention.

The requirement is still deemed proper and is therefore made FINAL.

4. Claim 24 is withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

5. Claims 18-23 are under examination as they read on an antibody with binding affinity to a protein encoded by SEQ ID NO: 12.

6. The specification on page 1 should be amended to reflect the status of 08/568,310 and 09/270,455 and their relationship with the instant application.

7. The specification is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. Fig. 1 on page 3, line 15-22 has described a bovine calcium-binding protein and the DNA sequence encoding it that each must have a sequence identifier. Further, Fig. 2 on page 3, line 23-32 has describe a bovine calcium-binding protein and the DNA sequence encoding it that each must have a sequence identifier. Correction is required.

8. The specification is objected to for failing to provide a brief description of each individual Figure. Figure 3 has panels labeled A and B that must be identified in the Brief Description of the Drawings as "Figures 3A and 3B", after which each individual panel must be separately described. Correction is required.

9. The specification is objected because the specification on page 2, lines 34-35, page 5, lines 9-10, 14-15, 19-20, 23-24, page 7, lines 11-12, page 11, lines 12-13, page 12, line 33-34, page 18, line 33-34 discloses that "the amino acid sequence shown in SEQ ID NO: 1 or 12. However, SEQ ID NO: 1 and 12 are nucleic acid sequences, which are limited to their nucleic acid components. Correction/clarification is required.

10. The U.S. Patents 6,313,267 and 5,976,832 cited on the PTO FORM 892 are issued from the parental applications serial No. 09/270,455 and 08/568,310, respectively.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 18-20 and 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 18 is indefinite for being dependent upon claim 1, which has been canceled.

B. Claim 18 is indefinite because the recitation of "the amino acid sequence listed in SEQ ID NO: 1 or 12" in canceled base claim 1 is indefinite because SEQ ID NO: 1 and 12 are nucleic acid sequences and limited to their nucleic acid components. Applicants have failed to point out how a nucleic acid of SEQ ID NOs: 1 and 12 would comprise an amino acid sequence.

C. The parenthesis "(especially squamous epithelial carcinoma)" in claim 22 is ambiguous, it is unclear whether the remark especially squamous epithelial carcinoma is claimed or not. It is unclear that the squamous epithelial carcinoma is an essential element of the claim.

D. Claim 21 is being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: what antigen the hybridoma recognizes.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 18-23 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody with binding affinity to a calcium-binding protein comprising an amino acid sequence encoded by SEQ ID NO: 1 or 12 for diagnosing inflammatory diseases, dermatosis and lung and skin cancer, a method for producing a monoclonal antibody, and a calcium-binging protein assay regent comprising said antibody; does not reasonably provide enablement for an antibody with binding affinity to a calcium-binding protein comprising an amino acid sequence which is "substantially identical" to "the amino acid sequence listed in SEQ ID NO:1 or 12" in canceled base claim 1 or a method for producing a monoclonal antibody with binding affinity to a any "calcium-binding protein", characterized by culturing a hybridoma producing said monoclonal antibody in claim 21, a diagnostic agent for inflammatory diseases, neoplastic diseases, especially squamous epithelial carcinoma, dermatosis or blood diseases, which comprises an antibody of claim 18, in claim 22. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Besides the amino acid sequences encoded by SEQ ID NO:1 (bovine BAAF1) or 12 (human BAAF1) , the specification fails to provide any guidance as to how to make and how to use any "calcium-binding protein" which is "substantially identical" to the amino acid sequence of SEQ ID NO:1 or 12, or a diagnostic agent for the neoplastic diseases, dermatosis or blood diseases.

The claimed invention encompasses antibodies with binding affinity to proteins which is substantially identical to the amino acid sequence encoded by SEQ ID NO: 1 or 12. The specification on page 5, lines 7-25 discloses that by "substantially identical" is meant that it is either exactly identical or is modified at one or a few amino acids while retaining the calcium-binding activity. Further the specification discloses that by "a few" means less than, for example, about 10% of the entire number of amino acids of the amino acid sequence listed in SEQ ID NO: 1 or 12. However, the specification is silent with respect to specifically which amino acids are critical to the claimed calcium-binding activity such that one skilled in the art could predict which species would fall within the scope of the claims. Further, the specification fails to provide any guidance on how to make any calcium-binding protein as claimed in claim 21 or any amino acid sequence which is "substantially identical" to the amino acid sequence encoded by SEQ ID NO: 1 or 12.

Claim 18 requires antibody to bind to amino acid sequences that are "substantially identical" to amino acid sequences encoded by SEQ ID NOs: 1 or 12. Besides the amino acid sequences encoded by SEQ ID NO: 1 or 12, the present specification fails to provide sufficient disclosure of amino acid sequences that are "substantially identical" to amino acids encoded by SEQ ID NO: 1 or 12 and maintain functional properties of the BAAF1 activity. The specification does not provide sufficient guidance as to which of the amino acids may be changed while BAAF1 functional activity is retained. The one of the uses of the claimed amino acid sequence is to make antibody then any change in the amino acid sequences encoded by SEQ ID NO: 1 or 12

would affect the binding affinity of the antibody. Colman *et al* in Research in Immunology (145(1):33-36, 1994) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza *et al* in Journal of Protein Chemistry (11(5):433-444, 1992) teach that single amino acid substitutions outside the antigenic site on a protein effect antibody binding.

Further, at issue where the claimed antibody would function as a diagnostic agent for all and every neoplastic diseases and blood diseases. The specification on page 39, line 33 through page 40 line 19 discloses the reactivity of anti-CAAF1 antibody with cancerous areas of lung and skin in which no CAAF1 protein immunoreactivity had been found when normal, and hyperexpression was confirmed in those tissues with pulmonary squamous-cell carcinoma with a strong tendency to cornification, squamous carcinoma of the skin, Bowen's disease (intraepithelial carcinoma) and senile keratosis (intraepithelial carcinoma). The specification further discloses that neutophils and macrophages infiltrating the lesion sites exhibited strong CAAF1 protein immunoreactivity. Further, the specification discloses that the differences on cancer cells and normal cells in immunoreactivityies aagainst the anti-CAAF1 antibody suggest the usefulness of the anti-CAAF1 antibody as a diagnostic agent for cancer. In addition, the immunoreactivity of neutrophils and macrophages against anti-CAAF1 antibody further suggests additional usefulness of the anti-CAAF1 antibody as a diagnostic agent for various inflammatory diseases.

The scope of claim 22 is that the claimed antibodies would diagnose all and every blood diseases or neoplastic diseases. However, sickle cell disease is a common inherited red blood disorder which cannot be diagnosed using the claimed antibody because the said antibody does not detect the presence of sickle haemoglobin, neither does it distinguish between sickle cell trait and sickle cell disorders. Similarity, hemophilia, Huntington's disease, cystic fibrosis, phenylketonuria, blood pressure, among others cannot be diagnose using the claimed antibody. Further, it is unpredicted whether the claimed antibody would diagnose all and every neoplastic diseases. Yamamura et al (1996) teach that CAAF1 gene expression may be altered in malignant neoplasms. Further study is required to determine whether CAAF1 is involved in malignant transformation. Furthermore, besides the squamous epithelial carcinoma of the lung and skin cancer, the specification fails to provide guidance on how to diagnose other non-epithelial cell derived neoplastic diseases such as sarcoma (mesenchymal), or fibroma (a benign neoplasm of fibroblast origin) because the specification does not disclose a nexus between such diseases and a change in the expression of BAAF1.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

15. Claims 18-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an antibody with binding affinity to a calcium-binding protein comprising an amino acid sequence encoded by SEQ ID NO: 1 or 12.

Applicant is not in possession of an antibody with binding affinity to a calcium-binding protein comprising an amino acid sequence which is "substantially identical" to "the amino acid sequence listed in SEQ ID NO:1 or 12" in canceled base claim 1 or a method for producing a monoclonal antibody with binding affinity to a any "calcium-binding protein", characterized by culturing a hybridoma producing said monoclonal antibody in claim 21, a diagnostic agent for inflammatory diseases, neoplastic diseases, especially squamous epithelial carcinoma, dermatosis or blood diseases, which comprises an antibody of claim 18, in claim 22.

Applicant has disclosed only amino acid encoded by SEQ ID NO: 1 or 12; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

16. The certified translation of the foreign priority paper of JAPAN 7-70468 and JAPAN 7-45564 filed on 10/28/1998, in the parent application No. 08/568,310 is acknowledged. Therefore, the foreign priority documents provide support for claims 18-23.

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated by Pardue *et al* (1983).

Pardue *et al* teach a method for producing a monoclonal antibody with binding affinity to a calcium-binding protein, characterized by culturing a hybridoma producing that produce the monoclonal antibody (see abstract in particular).

The reference teachings anticipate the claimed invention.

19. Claim 18-19 and 22-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Guignard *et al* (European Journal of Clinical Investigation, Vol:24, Supl. 2, pp.211, 1994), as is evidenced by Guignard *et al* (July 1995), Yamamura et al and the specification on page 2 lines 7-35.

Guignard *et al* (1994) teach a polyclonal antibody (anti-P8 or anti-MRP-8), identify an unknown protein of 6.5 kDa (P6). Guignard *et al* also teaches that the P6 protein identified by N-terminal amino acid sequence analysis appeared to be a new protein of the S100 family (calcium-binding proteins). Further, Guignard *et al* concluded that a new protein of 6.5 kDa belonging to the S100 family was evidenced in human neutrophils (see abstract in particular). While the Guignard et al is silent as to the "amino acid which is substantially identical to amino acid sequence listed in SEQ ID NO: 12" per se; P6 has the same N-terminal amino acid sequence encoded by SEQ ID NO: 12 as is evidenced by Guignard *et al* (1995) that the p6b N-terminal sequence (p6b) TKLEEHLEGIVNIFHQYSVR (see Figure 3, at page 398 in particular) which is 100% identical to amino acids 2-21 of the amino acid encoded by SEQ ID NO:12. Further evidence that the amino acid sequence encoded by SEQ ID NO: 12 is p6 protein came from Yamamura *et al* who teach that Guignard *et al* (1995) isolated and partially characterized a novel human calcium-binding protein that cross-reacted with an antibody against MRP8. Yamamura *et al* concluded that the identified N-terminal 20 amino acid sequence of the reported protein was identical to that of human CAAF1, suggesting that this protein is CAAF1 (encoded by SEQ ID NO:12) (see page 359, lines 4-8 in particular). SEQ ID NO: 12 encodes human CAAF1 as is evidenced by the specification on page 2, lines 7-35 that the human calcium-binding protein is CAAF1 encoded by SEQ ID NO: 12.

Claim 22 is included because an antibody is an antibody irrespective of its intended use.

The reference teachings anticipate the claimed invention.

20. Claim 18-20 and 22-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Kelly *et al* (J. Patho. 1989), as is evidenced by Guignard *et al* (Immunol Cell Biol. 1996 Feb;74(1):105-7), Guignard *et al* (July 1995) Yamamura et al and the specification on page 2 lines 7-35.

Kelly *et al* teach monoclonal antibodies to study the expression of calgranulins by keratinocytes in inflammatory dermatoses. Kelly *et al* also teach that calgranulins are intracellular calcium binding proteins which have inflammatory cytokine activity. Further, Kelly *et al* teach that MAC 387 monoclonal antibody that recognizes a molecule probable containing both calgranulin A and B (see abstract in particular). MAC 387 monoclonal antibody also binds amino acid sequence encoded by SEQ ID NO: 12, as is evidenced by Guignard *et al* (Feb 1996) that the immunoreactivity of MAC 387 was compared with that of a polyclonal antibody raised against purified MRP-8, but cross-reacting with MRP-14, and p6, a novel S100 protein. Under such conditions, Mac 387 was found to recognize the three S100 proteins (see abstract in particular). P6 has the same N-terminal amino acid sequence encoded by SEQ ID NO: 12 as is evidenced by Guignard *et al* (1995) teaches the p6b N-terminal sequence (p6b) TKLEEHLEGIVNIFHQYSVR (see Figure 3, at page 398 in particular) which is 100% identical to amino acids 2-21 of the amino acid encoded by SEQ ID NO:12.

Further evidence that the amino acid sequence encoded by SEQ ID NO: 12 is p6 protein came from Yamamura *et al* who teach that Guignard *et al* (1995) isolated and partially characterized a novel human calcium-binding protein that cross-reacted with an antibody against MRP8. Yamamura *et al* concluded that the identified N-terminal 20 amino acid sequence of the reported protein was identical to that of human CAAF1, suggesting that this protein is CAAF1 (encoded by SEQ ID NO:12) (see page 359, lines 4-8 in particular). SEQ ID NO: 12 encodes human CAAF1 as is evidenced by the specification on page 2, lines 7-35 that the human calcium-binding protein is CAAF1 encoded by SEQ ID NO: 12.

The reference teachings anticipate the claimed invention.

21. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 3, 2005

Maher Haddad

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Jasemine C. Chambers

JASEMINE C. CHAMBERS
DIRECTOR
TECHNOLOGY CENTER 1600